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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,441	12/18/2001	Michael Doenhoff	687-102	1683

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EXAMINER
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ART UNIT	PAPER NUMBER
1645	

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9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/020,441	Applicant(s) DOENHOFF ET AL.	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *12-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment filed on 3/25/2003, paper # 7 is acknowledged. Claims 1-17 are pending in the application.

Priority

2. This Application is a continuation of Application No. 09/413,810, abandoned. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Information Disclosure Statement

3. Information Disclosure Statement filed on 12/18/01 (Paper # 1) is acknowledged and a signed copy is attached to this Office action.

Drawings

4. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See attached PTO-948 for details. Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect may be deferred until after the examiner has considered the proposed drawing correction. Failure to timely submit the proposed drawing correction will result in the abandonment of the application.

Specification - Informalities

5. This application is informal in the arrangement of the specification. Applicant attention is directed to MPEP 608.01(a). For Example: Brief Description of the Drawing should be recited after Summary of the Invention.

Claims should begin with "I claim" or "We claim" or "What is claimed is".

Election/Restriction

6. Applicant's election of Group 1, Claims 1-11 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the composition and method of treatment are classified under same class, even though different subclass and search and examination would not be an undue burden. This is not found persuasive. . MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required. The term "distinct" is defined to "mean that two or more subjects as disclosed are related, for example, as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.01). In the instant situation, the inventions of the Groups are drawn to distinct inventions, which are related as product and process of use. (MPEP § 806.05(h)) states that the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product In the instant case the product as claimed could be used in other process such as immunoaffinity chromatography as set forth in the previous office action.

Concerning the burden of search and classification of subject matter is merely one indication of the burdensome nature of the search involved. The protein database search and the literature search for each of the inventions, both of which are particularly relevant in this art, are not co-extensive and are much more important in evaluating the burden of search. For example, search and examination issues for product and method of use are different. Clearly different searches and issues are involved in the examination of each group. Additionally, it is submitted that the inventions of the separate Groups have acquired a separate status in the art.

The requirement is still deemed proper and is therefore made FINAL.

7. Group I, claims 1-11 are under examination.

8. Claims 12-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claim Rejections - 35 U.S. C. 112, first paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-11 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

The claims are drawn to a vaccine composition comprising a recombinant fusion protein capable of eliciting immunity against Schistosoma parasites, comprising an amino acid sequence from 27/28kD cercarial elastase sequence gene of S.mansoni and active fragments, homologues and variants thereof fused to a protein selected from suitable bacterial, phage and viral proteins together with a pharmaceutical carrier. Further the fusion protein comprises a coding sequence SEQ.ID.NO: 1 or a homolog or variant fused to a bacterial, phage and viral protein together with a pharmaceutical carrier.

The specification broadly describes as part of the invention a gene coding for the 30 kDa Schistosoma mansoni cercarial protease was amplified using the polymerase chain reaction (PCR) from genomic DNA templates. Cloning and sequencing of several independent PCR clones revealed the presence of an intron additional to the one described in the original cloning of the gene. The 3 exons were cloned into expression vectors so that they could be expressed as separate glutathione-S-transferase (GST) translational fusions, Sm30 EX-1-GST, Sm30 EX-2-GST and Sm30 EX-3-GST. Recombinant bacteria carrying this expression plasmid expressed the fusion proteins (see examples 1-5). However, the specification does not teach a recombinant fusion protein active fragments, homologues and variants thereof 27/28kD cercarial elastase sequence gene of S.mansoni fused to a protein selected from suitable bacterial, phage and viral proteins together with a pharmaceutical carrier and a recombinant fusion protein homolog or variant comprising a coding sequence SEQ.ID.NO: 1 fused to a bacterial, phage and viral protein together with a pharmaceutical carrier. The actual biological function of the recombinant fusion protein Sm30-GST was described as an immunogenic composition. USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116). Thus, an immunogenic composition comprising a recombinant fusion protein Sm-30GST with a pharmaceutical carrier meets the written description provision of 35 U.S.C. 112, first paragraph for the reasons set forth below.

The specification fails to teach a recombinant fusion protein active fragments, homologues and variants thereof 27/28kD cercarial elastase sequence gene of S.mansoni

fused to a protein selected from suitable bacterial, phage and viral proteins together with a pharmaceutical carrier and a recombinant fusion protein homolog or variant comprising a coding sequence SEQ.ID.NO: 1 fused to a bacterial, phage and viral protein together with a pharmaceutical carrier and it is noted that the claimed fragments or homologs do not exist as an invention independent of their function. The actual structure or other relevant identifying characteristics of said recombinant fusion protein active fragments, homologues and variants thereof having the claimed properties as a vaccine were not described. There is no written description support for claimed recombinant fusion protein active fragments, homologues and variants thereof 27/28kD protease and a recombinant fusion protein homolog or variant comprising a coding sequence SEQ.ID.NO: 1 The specification fails to teach the structure or relevant identifying characteristics of a representative number of recombinant fusion protein active fragments, homologues and variants thereof 27/28kD protease protein and a recombinant fusion protein homolog or variant comprising a coding sequence SEQ.ID.NO: 1, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chuaai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

11. Claims 1-11 are also rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition comprising a recombinant fusion protein Sm30-GST comprising an amino acid sequence from 27/28kD cercarial elastase sequence comprising a coding sequence SEQ.ID.NO: 1 fused to a protein selected from suitable bacterial, phage and viral proteins together with a pharmaceutical carrier, the specification does not reasonably provide enablement for (1) a vaccine comprising a

recombinant fusion protein capable of eliciting immunity against Schistosoma parasites, comprising an amino acid sequence from 27/28kD cercarial elastase sequence gene of S.mansoni and (2) a recombinant fusion protein active fragments, homologues and variants thereof 27/28kD protease protein fused to a protein selected from suitable bacterial, phage and viral proteins together with a pharmaceutical carrier and (3) a recombinant fusion protein homolog or variant comprising a coding sequence SEQ.ID.NO: 1 fused to a protein selected from suitable bacterial, phage and viral proteins together with a pharmaceutical carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims since there is no written description support for the claimed invention.

The specification teaches a recombinant fusion protein Sm30-GST protein as an immunogenic composition. The specification teaches only about 44% of the worm burden is reduced when animals immunized with recombinant fusion protein Sm30-GSTand challenged with S.mansoni species only. However, the specification fails to teach that a recombinant fusion protein. Further, the specification does not teach a recombinant fusion protein active fragments, homologues and variants thereof 27/28kD protease protein fused to a protein selected from suitable bacterial, phage and viral proteins together with a pharmaceutical carrier and a recombinant fusion protein homolog or variant comprising a coding sequence SEQ.ID.NO: 1 fused to a protein selected from suitable bacterial, phage and viral proteins together with a pharmaceutical carrier. Serum from a rabbits immunized with Sm-30 GST was reactive against the native form of the 27/28kD protease and the expression product containing recombinant second exon, Sm30 EX-2-GST and the full length Sm30-GST. However, other two recombinant fusion proteins Sm30 EX-1-GSTand Sm30 EX-3-GST did not react (see figure 4) indicating that the recombinant fusion protein Sm-30 –GST comprises an immunogenic

component, Sm30 EX-2-GST, where in said immunogenic component binds to an antibody raised against full length Sm30-GST.

The state of the prior art indicates (see review article by Ross et al 2001, Clin. Microbiol. Rev, 14: 270-295) that various recombinant antigens were used as vaccine candidates together with adjuvants. However, none of the vaccine candidates confer protection against (Table 3 of Ross et al 2001) homologous (same) Schistosoma challenge infection. Sm30-GST, capable of eliciting protective immunity against genus Schistosoma (i.e., all species). The state of the prior art is decisive regarding the protective immunity involving both humoral and cell mediated immune response (see pages 286-287),The prior art further suggests that the protective efficacy of the recombinant vaccine candidates is to enhance the immunogenicity of the antigen by using adjuvants, combination of praziquantel treatment and coupling of cytokines and putative identification of T-cell antigens (see page 288) from a recombinant library etc. Thus, a recombinant vaccine composition capable of eliciting protective immunity against homologous Schistosoma challenge infection needs to be yet demonstrated. Therefore, a vaccine comprising a recombinant fusion protein comprising fragments, homologues and variants of 28kD elastase sequence and a recombinant fusion protein homolog or variant comprising a coding sequence SEQ.ID.NO: 1 against all Schistosma parasites must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case by case basis. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

Claim Rejections - 35 U.S. C. § 112, second paragraph

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

13. Claims 1-11 are rejected under 35 U.5.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected as being indefinite for the recitation of " active fragments " it is impossible to understand the metes and bounds of the term active fragments because it is not clear whether these fragments are active biochemically (i.e., enzymatically) or functionally.

Claims 3-5 are indefinite because the claims recites ' " at least a sequence". As claimed it is impossible to understand the metes and bounds of the term "at least. "

Claim 4 is rejected as being vague for the recitation of "amino acid residues 136-151 of the S.mansoni cercarial elastase molecule" because the fusion protein of claim 3,SEQ.ID.NO: 2 do not contain amino acid residues 136-151.

Claim Rejections - 35 USC 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

((b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1-11are rejected under 35 U.S.C. 102(b) as being anticipated by Price et al 1997.

The claims are drawn to a vaccine composition comprising a recombinant fusion protein capable of eliciting immunity against Schistosoma parasites, comprising an amino acid sequence from 27/28kD cercarial elastase sequence gene of S.mansoni and active fragments fused to a protein selected from suitable bacterial, phage and viral proteins together with a pharmaceutical carrier. Further the fusion protein comprises a coding sequence SEQ.ID.NO: 1,

amino acid sequence SEQ.ID.NO: 2 and 3 fused to a bacterial, phage and viral protein, wherein said fused protein is GST from S.japonicum together with a pharmaceutical carrier.

Price et al 1997 disclose a recombinant elastase fusion proteins, exon-GST fusion proteins pEXON1, pEXON2 and pEXON 3 (abstract and figure 2) comprising an amino acid sequence from 27/28kD cercarial elastase sequence gene of S.mansoni comprising a coding sequence SEQ.ID.NO: 1 (figure 1), said coding sequence comprising amino acid residues as represented by SEQ.ID.NO: 2 (see figure 1 line 5, starts with capital GTT (Val) – line 10, ends with AAG (Lys) and SEQ.ID.NO: 3 (figure 1, line 9 starts with capital GTT (Val) and with line 10, AAG (Lys). The recombinant clones contain elastase gene of S.mansoni fused to a 26 and 28kD GST of S. japonicum and were expressed as GST fusion proteins. The recombinant fusion protein comprising an amino acid sequence from 27/28kD cercarial elastase sequence gene of S.mansoni was fused to a GST protein and then expressed in E.coli. Clones carrying GST-exon fusions (see page 449, first paragraph) were identified by DNA sequencing by the use of cloned cells as a source of DNA (see page 449, upper left column). A small number of recombinant clones that express recombinant fusion protein were resuspended in 100-ul sterile filtered water, placed in a water bath at 100°C for three minutes. Therefore, the limitation pharmaceutically acceptable carrier read on sterile distilled water and thus recombinant clones that express recombinant fusion protein cells in sterile distilled water meet the claim limitations. The antigenicity of these three proteins was tested in Western blot analysis using antisera raised against S.mansion native protease and S. japonicum native GST. The recombinant proteins were recognized by both sera, where as GST alone was recognized by the anti-GST serum (see page 451, left column, under Antigenecity of recombinant proteins and figure 3). Limitations such as vaccine for oral administration, administration by injection, capable of

eliciting immunity against S. mansoni were treated as intended uses of vaccine. Therefore, the prior art anticipated the claimed invention.

It is acknowledged that weight is given to every term in claims. This is why the instant claims drawn to vaccines for eliciting immunity against Schistosoma is scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. If the vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. Of course, the existence of an unobvious structural difference would define over the prior art. Here, the prior art teaches the same recombinant antigens and formulations thereof as claimed.

Status of Claims

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D

4/30/03

PATRICIA A. DUFFY
PRIMARY EXAMINER